CASE REPORT

24(102), March - April, 2020

ISSN
2321–7359
EISSN
2321–7367

Medical Science

Coexistence of hypertriglyceredemia and hypercholesterolemia with gestational diabetes mellitus in pregnancy: A case report

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Article History
Received: 30 October 2019
Reviewed: 01/November/2019 *to* 12/December/2019
Accepted: 13 December 2019
Prepared: 15 December 2019
Published: March - April 2020

Citation
Saunitra A. Inamdar, Himanshi Agarwal, Sourya Acharya, Anil Inamdar. Coexistence of hypertriglyceredemia and hypercholesterolemia with gestational diabetes mellitus in pregnancy: A case report. *Medical Science*, 2020, 24(102), 594-598

ABSTRACT

Hypertriglyceridemia in pregnancy is a relatively rare entity. In patients with genetic susceptibility, it can be life threatening. Complications include hyperviscosity syndrome, acute pancreatitis and sometimes preeclampsia. Hypercholesterolemia is also

encountered in pregnancy. However, at present it is not routinely measured or treated. The effects of maternal high cholesterol on pregnancy and on foetal development are not yet fully understood. Diabetes is the most common medical complication of pregnancy. Diabetes can be classified in pregestational or overt, and those diagnosed during pregnancy gestational diabetes. We present a case of 24 years old pregnant female with hypertriglyceridemia, hypercholesterolemia along with gestational diabetes mellitus and pre-eclampsia who was managed medically with a successful maternal and foetal outcome.

Keywords: pregnancy, hyperlipidaemia, hypercholesterolemia, gestational diabetes, preeclampsia

1. INTRODUCTION

Cholesterol is required for metabolizing hormones, bile acids and vitamin D in each and every cell in the body. Human plasma cholesterol levels are determined by production in the liver and by dietary intake. Lipoprotein helps to carry cholesterol around the body, and facilitate its crossing across placenta. It is a known fact that lipid profile changes during pregnancy secondary to hormonal changes, but these rarely presents with clinical syndromes (Basaran A, 2009). An exception to this is pregnancy related hypertriglyceridemia (HTG), whose complications mentioned before (Ray JG et al., 2006), are life threatening but likely preventable with timely done interventions. Plasma triglycerides usually increases 2 to 4 fold in uncomplicated late gestation (Knopp RH et al., 1986), but for most women with normal baseline TG levels and no defects in metabolic pathways, such increase is well tolerated. However, in rare instances, genomic alterations affect key metabolic entities where pregnant women can develop hypertriglyceridemia, which is defined as plasma triglyceride levels greater than 11.4mmol/litre (1000 mg/dl). The rare subgroups of pregnant women develops severe HTG, show an increased risk of acute complications and are at risk of expressing hyperlipidemia in the future (Basaran A, 2009). In one reported case, no obvious genetic cause was identified, suggesting a possible role for non genetic secondary causes of HTG pregnancy (Eskandar O et al., 2007).

Physiological modifications and potential risk during pregnancy

There is a metabolic shift in mother's body of carbohydrate to lipid for energy to make glucose easily available for the foetus. Secondarily, there is an increase in cholesterol levels for production of steroid hormones in placenta. FELIC (Fate of Early Lesions In Children) study states that with hyperlipidemia there occurs acute atherosclerosis leading to hypercoagulable state in the uterine spiral arteries resulting in local thrombosis and placental infarctions leading to foetal compromise (Ryckman KK et al., 2015). Pregnancy consists of many physiological metabolic adaptations (Weissgerber TL et al., 2000). Pregnant women have increased peripheral insulin resistance, leading to higher levels of hormones in the circulation compared with the non-pregnant state (Hodson K et al., 2013). There is an increase in all the lipid fractions in maternal body (Meyer BJ et al., 2013; Emet T et al., 2013). These metabolic changes are required for adequate foetal growth and development (Weissgerber TL and Wolfe LA, 2006; King JC, 2000). The change of serum lipid fractions is physiological and results from increased insulin resistance, lipoprotein synthesis and lipolysis in adipose tissue which mobilizes fats to serve as an energetic supply for foetal growth (King JC, 2000). Normal physiological changes include an increase in triglycerides (TG), high density lipoproteins (HDL), and low-density lipoproteins (LDL) (Knopp RH et al., 1986). Changes in lipid metabolism ensure a continuous supply of nutrients to the foetus, despite the improper or decreased maternal food intake (Butte NF, 2000). However, the disturbances of lipid during pregnancy may also lead to an increased risk of Cardio Vascular Disease and results in poor maternal and foetal outcome (Emet T et al., 2013; Charlton F et al., 2014), such as preeclampsia (Charlton F et al., 2014; Spracklen CN et al., 2014), gestational diabetes mellitus (Ryckman KK et al., 2015; Wang C et al., 2016), intrauterine growth restriction and premature birth (Emet T et al., 2013; Pecks U et al., 2012). Some previous studies have showed that the most dramatic damage in the lipid and lipoprotein profile in normal pregnancy is serum TG, which may be as high as two or three folds (De J et al., 2006). Non-fasting triglycerides were reported to have a greater impact on risk of cardiovascular diseases than fasting triglycerides (Iso H et al., 2014; Egeland GM et al., 2009).

2. CASE REPORT

A 24 years old with 32 weeks of GA was referred with blood *dyscrasias* with bad obstetric history with gestational DM and pre-eclampsia with cervical stitch in situ done at 24 weeks of GA with polyhydramnios (Liquor Index-19). She had history of previous 2 abortions, with unknown cause. She had previous normal delivery with femalechild of 4 years of age. On admission her blood pressure was 150/90mmhg with urine albumin +1. Her fundus examination showed no evidence of hypertensive retinopathy. Her blood sugar levels (RBS-271mg/dL, FBS-380mg/dL, PMBS-522mg/dL, HBA1C-5.86) were raised with urine sugars +3 and were

started on Inj Insulin R on Sliding scale. Blood samples were milky white in colour and the plasma couldnot be separated (figure-1). Her haemoglobin was also measured by Sahlis' method. There was an increase in her Serum Triglyceride-7460mg/dL and Serum Cholesterol levels-1080mg/dL, HDL-50mg/dL, LDL90mg/dL. Her serum amylase-60U/L, serum lipase- 24U/L, ECG and 2DECHO were normal. Her Ultrasonography abdomen and pelvis was also normal. There was no evidence of pancreatitis. Her thyroid levels were normal. She was started on Tab. Finofibrate 160 mg once a day, Tab. Pravastatin20mg H/S and Tab. Labetolol 100mg BD was started for the same.

Patient was given normal trial of labour but then was taken for emergency cesarean section in view of non progression of labour and a Female Baby 2.6kg was extracted and was shifted to Neonatal Intensive Care Unit for observation and Random Blood Sugar charting. Post delivery all the blood samples were repeated and there was decrease in the levels of serum triglyceride and serum cholesterol. Follow up of the patient was continued and post delivery lipid profile follow up was taken and it came out to be normal as shown in the table.

Table 1 showing the serial Triglyceride and Cholesterol levels of the patient from admission to the day of discharge

Duration:	TRIGLYCERIDE (mg/dL)	TOTAL CHOLESTEROL (mmol/L)
Reference Values	<150mg/Dl	<200mg/dL
On admission	7460	1080
After 2 months	950	605
Post delivery (1 month)	462	240
post delivery (2 months)	120	210

Figure 1 showing the milky white colour of the blood.

3. DISCUSSION

Hypertriglyceridemia usually starts from third month ante partum and it keeps on increasing till 36 weeks of gestation with constant higher cholesterol levels for 6 months post delivery. The major risk factors of high TG levels are obesity, diabetes, oestrogen therapy, thyroid diseases, alcohol consumptionand use of certain other medications and genetic causes (King JC., 2000). Treatment consists of modifications in lifestyle as well as medical line of management for reduction of cholesterol levels to achieve physiologically normal cholesterol levels.

Treatment of hypertriglyceridemia has 2 main objectives: Severe hypertriglyceridemia (TG concentration >10mmol/L) associated with pancreatitis and global vascular disease (increased concentration of TG rich lipoproteins, increased non-HDL cholesterol, APoB, LDL cholesterol) should be kept in mind. Immediate steps to reduce TG levels are done to minimize the risk of pancreatitis. In mild to

moderate hypertriglyceridemia (TG concentration 2-10mmol/L) following methods are to be followed (Hodson K et al., 2013; Emet T et al., 2013). Diet and exercise are first line of management. The pharmacological therapy depends on the TG levels. In the first two trimesters, the effect of the hormonal changes is to direct lipids toward storage depots for use in later gestation. In the third trimester, oestrogen stimulates production of hepatic VLDL, reduces removal of TG by LPL in the liver and adipose tissue, and reduces post-heparin lipolytic activity. In contrast, endogenous TG substrates, free fatty acids, and adipose tissue lipolysis are augmented by human placental lactogen (Hopkins PN et al., 2011). In addition, increases in exogenous TG related to increased appetite and hyperphagia also contribute to increased TG plasma concentrations, with a presumed teleological role of ensuring adequate substrate for normal foetal development (Sacks FM et al., 2010).

Family was screened for the same but there was no case with similar complaints in the family. After delivery all the lipid profile got normal which suggested isolated hypertriglyceridemia. Our patient did not have tendon xanthomas or arcus which is usually seen in prolong chronic hypertriglyceridemia. Specific management modalities to consider are: 1) low-fat diet; 2) nutritional supplements; 3) oral prescription medications; 4) parenteral heparin; 5) insulin infusion in the context of hyperglycemia and 6) TPE

Pharmacological therapy for hypercholesterolemia management

Statins: Presently statins are the mainstay for hypercholesterolemia treatment but statins have shown teratogenic effect on animals (Langsted A and Nordestgaard BG, 2011). Specially if used in first trimester women can have determined the defects in CNS and unilateral limb anomalies and other congenital anomalies. Use of statin is based on the efficacy of LDL cholesterol reduction. According to newer studies pravastatin reduces the risk of preeclampsia in high risk women.

For hypertriglyceridemia following drug therapy is recommended

Fibrates: 1st line drug is based on baseline triglyceride concentration. It is especially for patients with TG >2-3mmol/L and HDL < 1mmol/L. (Hopkins PN et al., 2011) Nicotinic acid (NIACIN, vit B3) = 2-3gm/day. It will act as a therapeutic option for statin intolerant patients. Omega 3 fatty acids: 4gm/day. It reduces TG upto 30% based on baseline concentration and is also useful in prevention of Pancreatitis.

Bile acid sequestrants: Colesevelam/cholestyramine a category B drug. It can be used in pregnancy as it doesnot pass through systemic circulation.

Apheresis: Can be considered in pregnancy if there is CVD. (Sacks FM et al., 2010).

4. CONCLUSION

It has been assumed for decades that hyperlipidaemia in pregnancy is physiological and not atherogenic. However, high maternal cholesterol levels during pregnancy are now linked with increased risks of preterm delivery, gestational diabetes and preeclampsia, as well as the later development of atherosclerosis in offspring. Hypertriglyceridemia and hypercholesterolemia was known to complicate the pregnancy. Familial Hypertriglyceridemia should always be ruled out in such cases and the complications should be attended soon to prevent further morbidity of the same. Therapy should include a multidisciplinary team to address dietary fat restriction, appropriate supplements, and possible medications when needed. Admission to hospital is recommended in severe cases. We conclude that with all the possible treatment protocols complications are preventable with appropriate and timely intervention.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Informed Consent

Appropriate consent was taken from the patient before making the case report.

List of Abbreviations

TG: triglyceride; LPL: lipoprotein lipase; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein; CVD: cardio vascular disease; GA: gestational age; FBS: fasting blood sugar; RBS: random blood sugar; PMBS: post meal blood sugar; HbA1C: glycosylated haemoglobin.

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